Painless Thyroiditis Complicated by Acromegaly

Takatoshi Saito, Katsuyoshi Tojo and Naoko Tajima

Abstract

The serum thyroid stimulating hormone (TSH) level is decreased in acromegalic patients. Although this phenomenon is thought to be caused by the enhanced secretion of somatostatin which suppresses TSH production, it has not yet been proven. We describe a 60-year-old woman with acromegaly who showed a low concentration of TSH. We diagnosed her as painless thyroiditis based on an increased level of thyroglobulin, depressed radioactive iodine uptake (RAIU), normal vascularity and mild swelling of the thyroid, and normal T3, T4, free T3 and free T4 levels. To our knowledge, this is the second reported case of acromegaly complicated by painless thyroiditis. The differential diagnosis between central hypothyroidism and painless thyroiditis is so important. Since it is difficult to diagnose precisely based on only the data of a low level of TSH and normal levels of thyroid hormones, we consider that measurement of thyroglobulin and RAIU is necessary when the complication of painless thyroiditis is suspected.

Key words: silent thyroiditis, scintigraphy, central hypothyroidism, latent thyrotoxicosis


Introduction

Acromegalic patients frequently have associated thyroid disorders. In particular, non-toxic nodular or diffuse goiter and toxic nodular goiter are often observed (1). In addition, thyroid volume and vascularity are also increased in acromegaly (2, 3). These findings may suggest that in acromegalic patients growth hormone (GH) and/or insulin-like growth factor-I (IGF-I) have growth promotive effects on the thyroid. On the other hand, acromegaly rarely complicates autoimmune thyroid diseases such as Graves’ disease or Hashimoto’s thyroiditis.

It is commonly known that the serum thyroid stimulating hormone (TSH) level is decreased in acromegalic patients. The response of TSH to TSH releasing hormone (TRH) is lower in acromegaly than in prolactinoma (4). A previous report stated that acromegalic patients show low concentrations of TSH, free T4 and T4 compared with the control group, indicating central hypothyroidism (5). Although this phenomenon is thought to be the result of enhanced secretion of somatostatin which suppresses TSH production (4), it has not yet been proven.

Painless thyroiditis (silent thyroiditis) is a relatively un-common cause of thyrotoxicosis and a clinical syndrome that manifests as transient thyrotoxicosis followed by transient hypothyroidism (6). This thyroiditis tends to show mild thyrotoxicosis with predominance of thyroxin, elevated thyroglobulin level, depressed radioactive iodine uptake (RAIU) and slightly enlarged thyroid (7, 8). Autoantibodies including anti-thyroglobulin antibody and anti-thyroid peroxidase antibody are often positive, therefore, painless thyroiditis is considered to be likely a variant of Hashimoto’s thyroiditis (7).

Recently we encountered an elderly woman case of acromegaly with a low TSH level. We diagnosed her as painless thyroiditis based on an increased level of thyroglobulin, depressed RAIU, mild swelling of the thyroid, normal vascularity and normal T3, T4, free T3 and free T4 levels in spite of low TSH level. To our knowledge, this is the second reported case of acromegaly complicated by painless thyroiditis. The complication of painless thyroiditis in acromegaly is so rare, and we think that it is very important to diagnose precisely whether painless thyroiditis or central hypothyroidism due to somatostatin.


**Table 1. Endocrinological Provocation Data**

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<td>2.36</td>
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**Case Report**

A 60-year-old woman visited our hospital presenting with swelling of the thyroid. She had no significant previous history except for colon polypectomy and was a life-long non-smoker. She had been prescribed amlodipine (5 mg/day) for four years to treat hypertension. In the outpatient clinic, swelling of the nose, lips, hand and foot were pointed out. Magnetic resonance imaging (MRI) of the pituitary showed an elliptical tumor (data not shown). Ultrasound sonography of the thyroid disclosed a small adenoma in the left lobe and swelling of the thyroid (data not shown). Additionally, endocrinological examination showed elevation of GH and IGF-I, and a low level of TSH. Therefore, in order to examine for endocrinological disorders, she was admitted to our hospital.

On admission, her consciousness was clear. Her body temperature was 36.0 degrees centigrade, the pulse rate was 72/min, regular, and blood pressure was 118/78 mmHg. Her height was 158 cm and weight was 57 kg. As mentioned above, acromegalic feature was detectable. Exophthalmoses were not detected. Visual field was intact. Examination of the chest did not indicate abnormality. Neither hepatomegaly nor splenomegaly could be pointed out. There was no peripheral edema or decreased skin turgor. No neurological disorder was detected. Urinalysis and hematological tests showed no abnormality. Blood chemistries were as follows; aspartate aminotransferase 19 IU/L (normal range: 10-40); alanine aminotransferase 16 IU/L (5-40); cholinesterase 5,194 IU/L (3,200-6,800); alkaline phosphatase 313 IU/L (96-300); lactate dehydrogenase 166 U/L (130-235); total bilirubin 0.7 g/dL (0.2-1.3); total protein 6.9 g/dL (6.3-8.8); albumin 4.0 g/dL (3.5-5.2); creatine kinase 74 U/mL (55-160); amylase 104 IU/L (30-130); blood urea nitrogen 15 mg/dL (8-20); creatinine 0.44 mg/dL (0.4-0.9); fasting plasma glucose 100 mg/dL (70-130); HbA1c 5.9 % (4.2-5.8); serum Na 143 mmol/L (135-145); Cl 105 mmol/L (98-108); K 4.5 mmol/L (3.2-4.4); Ca 2.45 mmol/L (2.00-2.50); P 3.6 mg/dL (2.6-4.6); total cholesterol 207 mg/dL (120-219); triglyceride 110 mg/dL (30-149); LDL-cholesterol 114 mg/dL (70-139); C-reactive protein 0.1 mg/dL (0.3>).

Endocrinological tests were as follows: GH 6.84 ng/mL (0.17>); IGF-I 1,100 ng/mL (41-272); luteinizing hormone 28.7 mIU/mL (8.7-38); follicle stimulating hormone 60.7 mIU/mL (26.2-113.3); prolactin 8.8 ng/mL (3.6-12.8); adrenocorticotropic hormone (ACTH) 12.5 pg/dL (7.2-63.3); cortisol 8.7 µg/mL (4.0-18.3); TSH 0.09 µIU/mL (0.5-5.0); freeT4 1.27 ng/dL (0.9-1.7); freeT3 3.16 µg/mL (2.3-4.3); T3 1.17 ng/mL (0.8-1.6); T4 70.2 ng/mL (61.0-124.0); thyroglobulin 110 ng/mL (30-300); thyroxin binding globulin 15.0 µg/mL (12.0-30.0); urinary cortisol, 18.6 µg/day (11.2-80.3); Anti-TSH receptor, thyroid peroxidase and thyroglobulin antibodies were all negative. Diurnal rhythms of ACTH and cortisol were normal, and 1-mg dexamethasone treatment resulted in suppression of ACTH and cortisol levels. 75-g oral glucose tolerance test showed abnormal elevation of plasma glucose level and no suppression of GH release (Table 1). Treatment with octreotide acetate or bromocriptine mesylate significantly decreased the GH level (data not shown). TRH test showed a poor response of TSH (Table 1). The 3-hour RAIU with I-131 was 3%, indicating very low uptake (data not shown).

Based on these data, we diagnosed her as acromegaly, impaired glucose tolerance and painless thyroiditis. Regarding the GH-producing pituitary adenoma that caused acromegaly, we explained the therapeutic options of surgery or medication (octreotide acetate or bromocriptine mesylate), and she opted for surgical treatment. Therefore, transsphenoidal surgery for pituitary adenoma was performed. Plasma GH levels were promptly decreased and plasma IGF-I levels fell into the age- and gender-adjusted normal range and remained stable thereafter. Pathological examination of the specimen obtained in surgery revealed the existence of GHoma. In contrast to GH and IGF-I levels, TSH and free T4 levels fluctuated sharply (Fig. 1). Thyroid hormone levels in the clinical course were within the normal limit; therefore, anti-thyroid drug has not been prescribed to the present.
Figure 1. Clinical course of TSH and free T4 levels. Closed circles mean TSH and closed squares mean free T4. The day when the operation was performed is indicated by the arrow.

Discussion

Falaschi et al presented the equations obtained by multiple regression analysis between freeT3, freeT4 and TSH values, in normal subjects and in patients with subclinical hyper and hypothyroidism (9). Present patient’s data was in relative agreement with their data, when applied to the equation of hyperthyroidism (hyperthyroidism: TSH=0.42-0.08×freeT4-0.03×freeT3). In contrast to the equation of hyperthyroidism, the equation of hypothyroidism did not match at all (hypothyroidism: TSH=13.54-3.1×freeT4-1.23×freeT3). For example, when freeT3 (pg/mL) and freeT4 (ng/dL) levels as mentioned above were applied to each of the equation, calculated TSH (µIU/mL) levels in the equation of hyperthyroidism and hypothyroidism were 0.22 and 5.72, respectively. Since the actual measured level of TSH was 0.09, the error rate in the equations of hyperthyroidism and hypothyroidism were 59.1% and 98.4%, respectively [the error rate = (calculated level-actual measured level) / calculated level]. Other data also showed comparable results. This evidence supports that the present case suffered from thyrotoxicosis. In addition, it was conceivable that elevation of thyroglobulin level could not be central hypothyroidism. Moreover, the fluctuation of the two variables (Fig. 1), was not inconsistent with a diagnosis of painless thyroiditis (10). These data lead us to diagnose her as painless thyroiditis, despite the fact that the low level of TSH in acromegalic cases has been considered to be suppressed by the increase of somatostatin.

Yoshinari et al speculated that GH might have a direct stimulatory action on the thyroid secretion of T4 possibly via increased IGF-I (11). In the present case the IGF-I level was very high; therefore, it might upregulate T4 secretion from the thyroid. However, if thyroid hormone production increased through high concentration of IGF-I, it was estimated that RAIU would be augmented. Although T4 production might be not a little affected by IGF-I in this case, we concluded that suppressed TSH secretion was mainly regulated by destructive thyroiditis not hyperfunction of the thyroid.

In the present patient symptoms induced by thyrotoxicosis were not seen at all. Moreover, no autoantibodies such as anti-TPO antibody and anti-thyroglobulin antibody, frequently detected in patients with painless thyroiditis, were observed. A previous report indicated that symptoms of this sickness are lighter in comparison with other thyroiditis such as hashitoxicosis and subacute thyroiditis (7). Additionally, in some patients with painless thyroiditis such antibodies do not become positive (12). Therefore, these negative findings could not rule out that this patient suffered from painless thyroiditis.

Only one case was previously reported (Punnose et al) as painless thyroiditis concomitant with acromegaly (13). Their patient developed painless thyroiditis after discontinuation of corticosteroid treatment for hypopituitarism due to apoplexy. A similar case with painless thyroiditis followed by pituitary apoplexy was reported and the authors speculated an immunological mechanism related to the onset of painless thyroiditis (14). On the other hand, the present case had no history of steroid therapy and there were no findings to indicate that immunological abnormality was induced. Additionally, all thyroid antibodies in our case were negative. Our case may indicate that painless thyroiditis develops via a separate mechanism rather than an immunological disorder.

Treatment for central hypothyroidism in acromegalic cases is thought to be not necessary because it is very mild (5); whereas it was often necessary to treat with β-blocker and/or steroid since thyroid function in painless thyroiditis fluctuates over a short duration. Hence, the differential diagnosis between central hypothyroidism and painless thyroiditis is critical. It is difficult to diagnose precisely based on only the data of a low level of TSH and normal levels of thyroid hormones. We consider that measurement of thyroglobulin and RAIU is necessary when the complication of painless thyroiditis is suspected.
Acknowledgement

We are indebted to Dr. Takeki Yamane (Department of Gastroenterology and Hepatology) for introducing this patient to us and we wish to also thank Sachie Saito for excellent secretarial work.

References


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